a) administering the compound to be tested to a [non-human] transgenic [mammal] mouse, or [mammalian] cells derived from the transgenic [mammal] mouse, wherein the transgenic [mammal] mouse has a nucleic acid construct stably incorporated into the genome, wherein the construct comprises a promoter for expression of the construct in a mammalian cell and a region encoding an Aβ-containing protein, wherein the promoter is operatively linked to the region,

wherein the region comprises DNA encoding the Aβ-containing protein, wherein the Aβ-containing protein consists of all or a contiguous portion of a protein selected from the group consisting of

APP770, APP770 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, APP751, APP751 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, APP695, and APP695 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717,

wherein the Aβ-containing protein includes amino acids 672 to 714 of human APP,

wherein the promoter mediates expression of the construct such that $A\beta_{tot}$ is expressed at a level of at least 30 nanograms per gram of brain tissue of the [mammal] mouse when it is two to four months old, $A\beta_{1-42}$ is expressed at a level of at least 8.5 nanograms per gram of brain tissue of the [mammal] mouse when it is two to four months old, APP and APPα

A

combined are expressed at a level of at least 150 picomoles per gram of brain tissue of the [mammal] mouse when it is two to four months old, APPβ is expressed at a level of at least 40 picomoles per gram of brain tissue of the [mammal] mouse when it is two to four months old, and/or mRNA encoding the Aβ-containing protein is expressed to a level at least twice that of mRNA encoding the endogenous APP of the transgenic [mammal] mouse in brain tissue of the [mammal] mouse when it is two to four months old;

wherein the transgenic mouse develops plaques that stain with Congo red; and

detecting or measuring the Alzheimer's disease marker such that any difference between the marker in the transgenic [mammal] mouse, or by [mammalian] cells derived from the transgenic [mammal] mouse, and the marker in a transgenic [mammal, or by mammalian cells derived therefrom] mouse, to which the compound has not been administered, or by cells derived from the transgenic mouse to which the compound has not been administered, is observed,

wherein an observed difference in the marker indicates that the compound has an effect on the marker.

7. (Amended) The method of claim 1 wherein the Alzheimer's disease marker is a protein and the observed difference is an increase or decrease in the amount of the protein present in the transgenic [mammal, or in mammalian cells derived therefrom] mouse to which the compound has been administered, or by cells derived from the transgenic mouse to which the compound has been administered.

9. (Amended) The method of claim 1 wherein the Alzheimer's disease marker is a protein and the observed difference is a reduction or absence of the protein in plaques or neuritic tissue present in the transgenic [mammal] mouse to which the compound has been administered.

11. (Amended) The method of claim 1 wherein the Alzheimer's disease marker is a protein and the observed difference is an increase or decrease in the enzymatic or biochemical activity of the protein in the transgenic [mammal, or in mammalian cells derived therefrom] mouse to which the compound has been administered, or by cells derived from the transgenic mouse to which the compound has been administered.

13. (Amended) The method of claim 1 wherein the Alzheimer's disease marker is a nucleic acid encoding a protein and the observed difference is an increase or decrease in the amount of the nucleic acid present in the transgenic [mammal, or in mammalian cells derived therefrom] mouse to which the compound has been administered, or by cells derived from the transgenic mouse to which the compound has been administered.

15. (Amended) The method of claim 1 wherein the Alzheimer's disease marker is a behavior and the observed difference is a change in the behavior observed in the transgenic [mammal] mouse to which the compound has been administered.

17. (Amended) The method of claim 1 wherein the Alzheimer's disease marker is a histopathology and the observed difference is a decrease in the extent or severity of the

histopathology present in the transgenic [mammal] mouse to which the compound has been administered.

19. (Amended) The method of claim 1 wherein the Alzheimer's disease marker is cognition and the observed difference is a change in the cognition of the transgenic [mammal] mouse to which the compound has been administered.

26. (Amended) The method of claim 1 wherein the promoter mediates expression of the construct such that $A\beta_{tot}$ is expressed at a level of at least 30 nanograms per gram of hippocampal or cortical brain tissue of the [mammal] mouse when it is two to four months old, $A\beta_{1-42}$ is expressed at a level of at least 8.5 nanograms per gram of hippocampal or cortical brain tissue of the [mammal] mouse when it is two to four months old, APP and APPα combined are expressed at a level of at least 150 picomoles per gram of hippocampal or cortical brain tissue of the [mammal] mouse when it is two to four months old, APPβ is expressed at a level of at least 40 picomoles per gram of hippocampal or cortical brain tissue of the [mammal] mouse when it is two to four months old, and/or mRNA encoding the Aβ-containing protein is expressed to a level at least twice that of mRNA encoding the endogenous APP of the transgenic [mammal] mouse in hippocampal or cortical brain tissue of the [mammal] mouse when it is two to four months old.

Please cancel claims 21 and 27.

Please add the following new claims.

28. (New) The method of claim 1 wherein the region encoding an Aβ-containing protein does not consist of a combination of APP cDNA encoding exons 1-6 and 9-18 and genomic APP sequences encoding introns 6, 7 and 8, and exons 7 and 8.

29. (New) The method of claim 1 wherein the Alzheimer's disease marker is selected from the group consisting of $A\beta_{tot}$, $A\beta_{1-42}$, $A\beta_{1-40}$, $A\beta_{N3}(pE)$, $A\beta_{X-42}$, $A\beta_{X-40}$, $A\beta_{Insoluble}$, $A\beta_{Soluble}$, full length APP, APPα, APPβ, FLAPP+ APPα, the last 100 amino acids of APP, and the last 57 to 60 amino acids of APP.

30. (New) The method of claim 17 wherein the Alzheimer's disease marker is selected from the group consisting of APP695, APP751, and APP770, and wherein the change in histopathology is a reduction in the amount of Alzheimer's disease marker localized in plaques and neuritic tissue.

31. (New) The method of claim 1 wherein the construct further comprises an effective amount of at least one intron, wherein the effective amount of at least one intron is located in the region of the construct encoding the Aβ-containing protein.

32. (New) The method of claim 30 wherein the intron is an APP gene intron.

33. (New) A method for screening compounds for an effect on an Alzheimer's disease marker comprising

a) administering the compound to be tested to a transgenic mouse, or cells derived from the transgenic mouse, wherein the transgenic mouse has a nucleic acid construct stably incorporated into the genome, wherein the construct comprises a promoter for expression of

the construct in a mammalian cell operatively linked to a region of the construct encoding a human amyloid precursor protein,

wherein the region of the construct encoding a human amyloid precursor protein is selected from the group consisting of APP770 cDNA; APP770 cDNA bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; APP751 cDNA; APP751 cDNA bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; APP695 cDNA; the APP695 cDNA bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; APP695, APP751, or APP770 cDNA truncated at amino acid 671 or 685; APP cDNA truncated to encode amino acids 646 to 770 of APP; a combination cDNA/genomic APP gene construct; a combination cDNA/genomic APP gene construct bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; and a combination cDNA/genomic APP gene construct truncated at amino acid 671 or 685;

wherein Aβ is expressed at a level of at least 50 ng/g brain tissue in the transgenic mouse when the transgenic mouse is three months of age;

wherein the transgenic mouse develops plaques that stain with Congo red; and

detecting or measuring the Alzheimer's disease marker such that any difference between the marker in the transgenic mouse, or by cells derived from the transgenic mouse, and the marker in a transgenic mouse to which the compound has not been administered, or

by cells derived from the transgenic mouse to which the compound has not been administered, is observed,

wherein an observed difference in the marker indicates that the compound has an effect on the marker.

34. (New) The method of claim 33 wherein the Alzheimer's disease marker is a protein and the observed difference is an increase or decrease in the amount of the protein present in the transgenic mouse to which the compound has been administered, or in cells derived from the transgenic mouse to which the compound has been administered.

35. (New) The method of claim 34 wherein the protein is selected from the group consisting of Cat D,B, Neuronal Thread Protein (CSF), nicotine receptors, 5-HT_2 receptor, NMDA receptor, α2-adrenergic receptor, synaptophysin, p65, glutamine synthetase, glucose transporter, PPI kinase, GAP43, cytochrome oxidase, calbindin, adenosine A1 receptors, choline acetyltransferase, acetylcholinesterase, glial fibrillary acidic protein (GFAP), α1-antichymotrypsin, α1-antitrypsin, C-reactive protein, α2-macroglobulin, IL-1, TNFα, IL-6, HLA-DR, HLA-A, D,C, CR3 receptor, MHC I, MHC II, CD 31, CR4, CD45, CD64, CD4, spectrin, tau, ubiquitin, MAP-2, apolipoprotein E, glycosylation end products, amyloid P component, laminen, and collagen type IV.

36. (New) The method of claim 33 wherein the Alzheimer's disease marker is a protein and the observed difference is a reduction or absence of the protein in plaques or neuritic tissue present in the transgenic mouse to which the compound has been administered.

37. (New) The method of claim 36 wherein the protein is selected from the group consisting of Cat D,B, protein kinase C, NADPH, C3d, C1q, C5, C4bp, C5a-C9, tau, ubiquitin, MAP-2, neurofilaments, heparin sulfate, chrondroitin sulphate, apolipoprotein E, glycosylation end products, amyloid P component, laminen, and collagen type IV.

38. (New) The method of claim 33 wherein the Alzheimer's disease marker is a protein and the observed difference is an increase or decrease in the enzymatic or biochemical activity of the protein in the transgenic mouse to which the compound has been administered, or in cells derived from the transgenic mouse to which the compound has been administered.

39. (New) The method of claim 38 wherein the protein is selected from the group consisting of nicotine receptors, 5-HT_2 receptor, NMDA receptor, α2-adrenergic receptor, glutamine synthetase, glucose transporter, PPI kinase, cytochrome oxidase, calbindin, adenosine A1 receptors, choline acetyltransferase, acetylcholinesterase, glial fibrillary acidic protein (GFAP), α1-antichymotrypsin, α1-antitrypsin, C-reactive protein, α2-macroglobulin, IL-1, TNFα, IL-6, HLA-DR, HLA-A, D,C, CR3 receptor, MHC I, MHC II, CD 31, CR4, CD45, CD64, CD4, spectrin, ubiquitin, and apolipoprotein E.

40. (New) The method of claim 33 wherein the Alzheimer's disease marker is a nucleic acid encoding a protein and the observed difference is an increase or decrease in the amount of the nucleic acid present in the transgenic mouse to which the compound has been

administered, or in cells derived from the transgenic mouse to which the compound has been administered.

41. (New) The method of claim 40 wherein the protein is selected from the group consisting of growth inhibitory factor, Cat D,B, Neuronal Thread Protein (CSF), nicotine receptors, 5-HT_2 receptor, NMDA receptor, α2-adrenergic receptor, synaptophysin, p65, glutamine synthetase, glucose transporter, PPI kinase, GAP43, cytochrome oxidase, calbindin, adenosine A1 receptors, choline acetyltransferase, acetylcholinesterase, glial fibrillary acidic protein (GFAP), α1-antichymotrypsin, α1-antitrypsin, C-reactive protein, α2-macroglobulin, IL-1, TNFα, IL-6, HLA-DR, HLA-A, D,C, CR3 receptor, MHC I, MHC II, CD 31, CR4, CD45, CD64, CD4, spectrin, tau, ubiquitin, MAP-2, apolipoprotein E, glycosylation end products, amyloid P component, laminen, and collagen type IV.

42. (New) The method of claim 33 wherein the Alzheimer's disease marker is a behavior and the observed difference is a change in the behavior observed in the transgenic mouse to which the compound has been administered.

43. (New) The method of claim 42 wherein the behavior is selected from the group consisting of behavior using working memory, behavior using reference memory, locomotor activity, emotional reactivity to a novel environment or to novel objects, and object recognition.

44. (New) The method of claim 33 wherein the Alzheimer's disease marker is a histopathology and the observed difference is a decrease in the extent or severity of the

histopathology present in the transgenic mouse to which the compound has been administered.

45. (New) The method of claim 44 wherein the histopathology is selected from the group consisting of compacted plaques, neuritic dystrophy, gliosis, Aβ deposits, decreased synaptic density, and neuropil abnormalities.

46. (New) The method of claim 44 wherein the Alzheimer's disease marker is selected from the group consisting of APP695, APP751, and APP770, and wherein the change in histopathology is a reduction in the amount of the marker localized in plaques and neuritic tissue.

47. (New) The method of claim 33 wherein the Alzheimer's disease marker is cognition and the observed difference is a change in the cognition of the transgenic mouse to which the compound has been administered.

48. (New) The method of claim 33 wherein the marker is detected or measured using RT-PCR, ELISA, antibody staining, laser scanning confocal imaging, and immunoelectron micrography.

49. (New) The method of claim 33 wherein the codon encoding amino acid 717 is mutated to encode an amino acid selected from the group consisting of Ile, Phe, Gly, Tyr, Leu, Ala, Pro, Trp, Met, Ser, Thr, Asn, and Gln.

50. (New) The method of claim 49 wherein the codon encoding amino acid 717 is mutated to encode Phe.